CLAIMS

1. Contrast agents for use in diagnostic ultrasound studies comprising microbubbles of gas or a gas precursor encapsulated in a protein shell characterised in that the said protein is crosslinked with crosslinking groupings containing biodegradable linkages.

2. Contrast agents as claimed in claim 1 wherein the crosslinking groupings contain biodegradable linkages selected from amide, imide, imine, ester, anhydride, acetal, carbamate, carbonate, carbonate ester and disulphide groups.

3. Contrast agents as claimed in claim 2 wherein the crosslinking groups contain biodegradable linkages of formula

$$-(Y)_n-CO-O-C(R^1R^2)-O-CO-(Z)_n-$$

(where Y and Z, which may be the same or different, are -O-, -S- or $-NR^3-$; R^1 and R^2, which may be the same or different, are hydrogen atoms or carbon-attached monovalent organic groups or together represent a carbon-attached divalent organic group; R^3 is a hydrogen atom or an organic group; and the symbols n, which may be the same or different, are zero or 1).

4. Contrast agents as claimed in any of the preceding claims wherein the protein is albumin, gelatin or globulin.

5. Contrast agents as claimed in claim 4 wherein the protein is human serum albumin.

6. Contrast agents as claimed in any of the preceding

claims further containing an inorganic particulate stabiliser.

7. A process for the preparation of a contrast agent as claimed in claim 1 which comprises encapsulating a gas or gas precursor in a protein and crosslinking the protein with crosslinking groups containing biodegradable linkages before, during or after said encapsulation.

8. A process as claimed in claim 7 wherein crosslinking is effected after encapsulation.

9. A process as claimed in claim 7 or claim 8 wherein crosslinking is effected using a crosslinking agent of formula (I)

$$A^1 - X - A^2 \qquad (I)$$

(where X is a linking group containing one or more biodegradable linkages as defined in claim 2 or claim 3 and A^1 and A^2, which may be the same or different, are functional groups reactive with proteins).

10. A process as claimed in claim 9 in which A^1 and A^2 are both aldehyde groups.

11. A process as claimed in any of claims 8 to 10 wherein encapsulation is effected by agitation or sonication of the protein in an aqueous medium to yield a protein foam which is dried and thereafter suspended in a solution of the crosslinking agent in a polar organic solvent.

12. A process as claimed in claim 11 in which the crosslinking agent is a compound of formula (I) as defined in claim 9 in which A^1 and A^2 are both O-linked sulphonated N-hydroxysuccinimidyl residues.